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copy for Joshua Lederberg

Prof. L. L. Cavalli-Sforza,
Department of Genetics,
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Stanford, California, 94305
USA

12 May 1992

Dear Professor Cavalli,

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I am writing this letter to tell you a story in which, quite unwillingly, I became interested in early results of E.coli genetics and arrived to the conclusion that your original idea of whole genome interaction between mating bacteria, even in the light of the one way transfer concept, might be revitalized as a real alternative concept.

The past few years in order to understand anomalies observed in our mapping studies via fusion of Bacillus megaterium protoplasts computerized model experiments were devised. Since in the fused bacterial protoplasts whole genome of both bacteria are present, the model progeny populations were constructed as though they had been obtained from free recombination of two parental genomes. Furthermore, since selection for two markers (one from each parent) is the standard procedure to obtain recombinant populations from such a cross, selections were performed accordingly. In a model system, clearly, all possible selections can be made. Thus, I have had an opportunity to clarify by model experiments what rules are operating when genetic analysis is made from samples selected for two markers. We had only then understood what is the trouble with the fusion mapping.

Meantime, in order to check the reliability of the model experiments the mating system of Streptomycets was taken, and some of David Hopwood and his school's published data were entered into the computer. The computer analysis then confirmed that the model functions according to the requirements of a real genetic system, too. Or, if you like, the model experiments basically confirmed David Hopwood's concept of Streptomycetes genetics, where in the mating process whole genome interactions are envisaged. It also revealed some problems related to his mapping procedure, which I have already discussed with him.

In the possession all of these experiences I had recalled the early ages of Escherichia coli genetics where Joshua Lederberg, you, as well as a few other scholars were looking for the data as though the recombinant population had been obtained by whole genome interaction of the parents. I went trough all those early papers available here and concluded that the anomalies observed in those mapping studies can be explained in the knowledge of the rules how selected samples of recombinants behave in the genetic analysis (which you could not be aware of in that time).

Then, just for the sake of the intellectual pleasure, it was looked for how the model selected samples behaved when they are examined according to the logic which resulted in the general acceptance of the unidirectional, partial information transfer concept. Thus, the evidences and argumentation of Élie Wollman and Francois Jacob as described in "La Sexualité des Bactéries" were taken and examined. It

turned out, to my greatest astonishment, that when in the selected samples (obtained from a progeny of whole genome interaction) only alleles from one of the parents are taken into consideration (as it is made according to the one way transfer concept), then the data can only be interpreted in a comprehensive way if it is hypothesized that the sample is obtained by an one way partial transfer of information (i.e. the effects of selections are explained by the way of information transfer).

In the early times, as you remember, to understand the genotype structure of selected samples post-zygotic or pre-zygotic elimination of genotypes were considered. The selection as distorting the genotype composition of sample was clearly realized, even though its differential elimination effect on genotypes as a third alternative was not envisaged in the evaluation of the genotype composition of a selected sample. Thus, the peculiarities of early selected samples obtained from the crosses could as well be interpreted by the peculiarity of behaviour of selected samples from a progeny where whole genome interaction was operating.

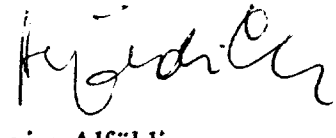
Nevertheless, in the light of the streptomycin effect on the polarity of the cross demonstrated by Bill Hayes all these model data seemed to us mere coincidences by chance. Thus, just for the sake of curiosity we have repeated the Hayes experiment. Indeed, one mg/ml streptomycin treated overnight culture of Hfr Cavalli gave TL recombinants with the PA309. Even though, it was difficult to accept that killed Hfr may be active, thus the streptomycin was washed out and the treated culture plated to see if there are yet colony formers. There were. To be short: Recombinants can only be obtained with a streptomycin treated Hfr if there are survivors (persisters) in the culture. Our conclusion: The Hayes experiment, may be, is not as fail safe proof for the unidirectional transfer concept as generally accepted.

Recently I had an opportunity to show results of my model experiments to Francois Jacob. It was my impression that he acknowledged great majority of my efforts as an intellectual tour de force: how circularity of chromosome is obtained from a linear chromosome just taking a few appropriate selections from the same progeny or how "time of marker entry" mapping can be achieved by the whole genome interaction model, too. Nevertheless, he finds probably all of these possibilities far from the realty.

In any case it is amazing how the seemingly alien Streptomyces and Coli-type genetics can be unified on an intellectual level by the model experiments.

Finally I may add that I have made a writing about all of the above mentioned model experiments in the form of a primitive and long manuscript (with the tables more than 100 typed pages). In the age of recent technological and intellectual developments of the molecular genetics it is probably written for my drawer. Since I do not know if you find some value in trying to go back to such "outdated" problems, and question the validity of the one way transfer mechanism, unquestionable concept in the past decades, I do not annoy you wit the manuscript. Anyhow, I sincerely hope the account of my story at least reminds you of the golden age of your youth.

Sincerely yours,



Lajos Alföldi